

SHORT REPORT

Eyelid tremor in a patient with a unilateral paramedian thalamic lesion

G J Jungehülsing, C J Ploner

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A patient with a circumscribed infarction of the right paramedian thalamus developed a tremor of both eyelids on voluntary eye closure. Co-registration of the magnetic resonance image to a stereotactic atlas of the human thalamus revealed that the lesion was confined to a small subgroup of paramedian nuclei, including the parvocellular part of the mediodorsal nucleus. It is concluded that this region provides inhibitory input to cortical and/or subcortical regions controlling eyelid movements. Voluntary eye closure may involve direct cortico-nuclear connections and indirect pathways through the paramedian thalamus, most probably through the mediodorsal nucleus.

Involuntary movements of the eyelids are an underdiagnosed neuro-ophthalmological sign, occurring with several neurological disorders.^{1–4} However, the value of such signs for localisation of pathological processes within the central nervous system is still unclear, probably because current knowledge of the neural control of eyelid movements is largely confined to the brain stem.^{5–6} We report a case of eyelid tremor in a patient with a unilateral ischaemic lesion of the paramedian thalamus, suggesting that this region is involved in supranuclear control of voluntary eyelid movements.

CASE REPORT

Patient

A 27 year old man presented after having noticed “difficulties in waking up”. Later that day he noticed a sustained “lid hopping” during eyelid closure. This “fluttering” of eyelids on eye closure persisted, and he noted that it could be intensified by “excitement” or by “thinking of stressful things”. Further details of the patient’s medical history included Fallot’s pentalogy and a small abscess in the right temporal lobe attributable to bacterial endocarditis 10 years before admission. No further history of neurological disorders was reported. On initial clinical examination, impaired vigilance was found, which resolved within a few hours. As soon as the patient closed his eyes, both eyelids showed sustained bilateral synchronous twitching movements. These rapid eyelid jerks were independent of convergence, direction of gaze, or brightness of the environment, but could be suppressed by forceful eye closure and disappeared with sleep. Clinically, there was no evidence of vertical eye movements accompanying the patient’s involuntary eyelid twitches. No further neurological deficits were found. Bedside testing revealed full range conjugate ocular motility and normal saccades and pursuit eye movements. There was no evidence of spontaneous or gaze evoked nystagmus, square wave jerks, ptosis or lid retraction and no other involuntary movements were observed. The condition remained unchanged during a follow up of 13 months.

Magnetic resonance imaging

Acute diffusion weighted and perfusion weighted MRI showed a solitary ischaemic lesion affecting the right paramedian thalamus.

Later, horizontal and sagittal T1 weighted and T2 weighted MRI (fig 1A, B) and high resolution TIRM-MRI (time inversion recovery magnetisation; fig 1C) was performed, confirming that the lesion was confined to the thalamus and did not extend into the midbrain. With the exception of a small residual lesion attributable to the patient’s temporal lobe abscess 10 years before admission, which had already been present on several previous MRIs, no further lesions were found. Co-registration of TIRM-MRI to a digitalised, three dimensional stereotactic atlas of the human thalamus⁷ revealed that the patient’s thalamic lesion affected mainly the parvocellular division of the mediodorsal nucleus (MDpc) and the paraventricular and parafascicular nuclei. The lesion was adjacent to the central lateral nucleus, the subparafascicular nucleus, the ventral medial nucleus, the central medial nucleus, and the medial ventral nucleus.^{7,8}

Clinical neurophysiology

Firstly, the patient’s eyelid tremor was recorded with a conventional videocamera. Frame by frame analysis of the video revealed a fairly regular tremor frequency of about 7 Hz. Subsequent electro-oculography (EOG) did not show any pronounced spontaneous abnormal eye movements during eye closure, although small vertical eye movements may have been undetected because of the tremulous muscular activity reported below. As the patient was treated with anticoagulants, needle electromyography (EMG) of the levator palpebrae muscle (LP) and orbicularis oculi muscle (OO) could not be performed. Hence, EMG from the right upper eyelid was recorded with EOG electrodes. The recording electrode was placed midline over the upper eyelid, close to the junction of the orbital and palpebral parts of the OO. With eyes open, brief bursts (about 100 ms duration) of EMG activity occurred at a regular frequency of 3 Hz (fig 2). These bursts were not detectable by clinical observation. Between these bursts, no EMG activity was observed, suggesting that tonic LP activity with eyes open⁶ was not sampled by the EOG electrode. EMG activity is thus likely to represent contractions of the OO. Immediately on eye closure, much shorter bursts of muscle activity occurred at a regular frequency of 13 Hz (fig 2), accompanying the clinically detectable 7 Hz eyelid jerks reported above. Amplitude of these bursts was unrelated to convergence or direction of gaze and remained constant as long as the eyes were closed. Amplitude of bursts did not increase with eye closure (fig 2). Thus, clinically detectable lid movements on eye closure are probably attributable to tremulous contractions of the LP, with the EMG signal representing clinically inapparent tremulous contractions of the OO. Opening of the eyes stopped this high frequency EMG activity.

Abbreviations: MDpc, mediodorsal nucleus; EOG, electro-oculography; EMG, electromyography; LP, levator palpebrae muscle; OO, orbicularis oculi muscle

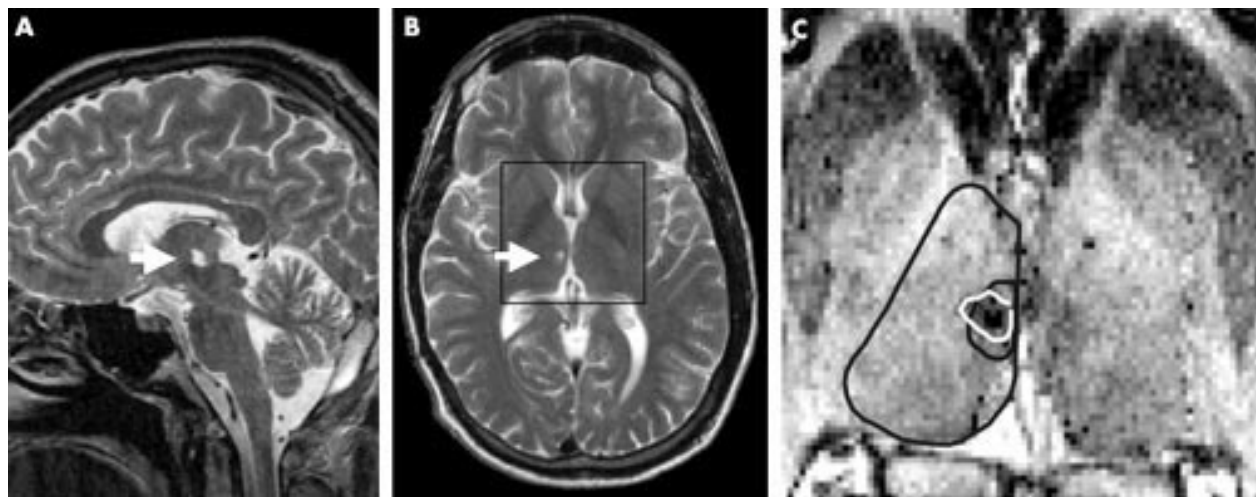


Figure 1 T2 weighted sagittal (A) and horizontal (B) MRI showing a lesion to the right paramedian thalamus (arrows). (C) TIRM-MRI with thalamic anatomy according to reference 7. Outer black line: thalamus; inner black line: parvocellular division of mediodorsal nucleus (MDpc); white line: lesion extent.

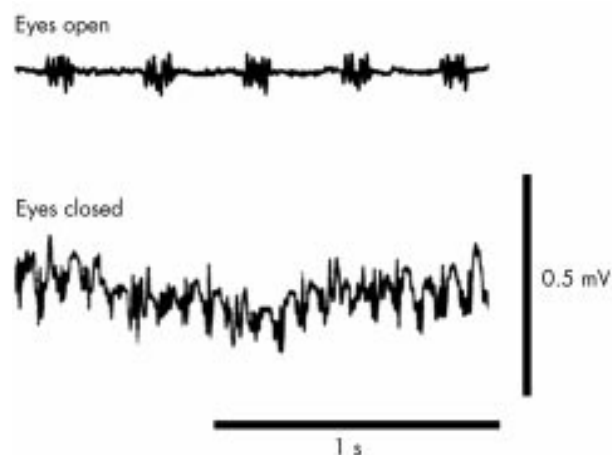


Figure 2 Surface electromyograms recorded with Ag-AgCl electrodes from the right upper eyelid of the patient.

immediately. Results from auditory evoked potentials, blink reflexes, and electroencephalography were completely normal.

DISCUSSION

A 27 year old man with an ischaemic lesion of the right paramedian thalamus developed rapid, symmetrical, and sustained involuntary movements of the eyelids on voluntary eye closure. Apart from impaired vigilance at onset, a well known sign of paramedian thalamic infarcts,⁹ no further neurological deficits were observed. As the rhythmical jerks of our patient's eyelids were not precipitated by slow downward drifts and independent of convergence or direction of gaze, the condition is different from cases of eyelid nystagmus reported previously.² Furthermore, our patient showed no associated ocular nystagmus or signs of midbrain, medullary, or cerebellar disease, which frequently accompany eyelid nystagmus.^{2,6,10} The frequency of the patient's eyelid twitches (about 7 Hz) further differs from blepharoclonus—that is, repetitive jerks of the eyelids, frequently induced by eye closure, but occurring with frequencies of about 2–4 Hz.³ With regard to their regularity and their movement characteristics, we term our patient's involuntary lid movements eyelid tremor.

Involuntary movements of the eyelids have been described occasionally with lesions affecting the thalamus.^{4,11,12} Among

these cases, a patient with bilateral ischaemic lesions confined to the paramedian thalamus is reported, who showed incapacitating bilateral involuntary eyelid movements, which may well represent a severe variant of the eyelid tremor observed here.¹² MRI shows that this patient's right sided lesion corresponds very closely to the lesion in our case. However, an additional and slightly different lesion to the left paramedian thalamus renders a direct comparison to our patient difficult. This applies also to the other three cases, where additional lesions and neurological deficits preclude unequivocal inferences on the affected thalamic nuclei.^{4,11}

Normally, eyelid movements result from antagonistic activity of LP and OO, which reciprocally inhibit each other.⁶ Involuntary eyelid movements may therefore result from inappropriate excitation or inhibition of LP or OO, or both.¹ In our patient, there was inappropriate OO activity with eyes open and inappropriate LP activity with eyes closed. The discrepancy between frequency of contractions in LP and OO further suggests that reciprocal inhibition between both muscles was impaired. Because an ischaemic lesion should result in loss of function, disinhibition rather than abnormal excitation of OO and LP is the most probable explanation for these findings. It may be assumed that lesion to the paramedian thalamus has led to a loss in inhibitory control of cortical and/or subcortical premotor structures involved in eyelid movements.

At the cortical level, functional imaging studies in humans and electrophysiological studies in monkeys indicate that frontal regions largely congruent with the supplementary eye field and the frontal eye field, are involved in eyelid movements.^{13,14} Both regions project directly on the periaqueductal grey,^{15–17} that is, the region that provides tonic input to LP motoneurons in the unpaired central caudal nucleus for sustaining the open eyelid position.^{5,6} As these projections travel through the internal capsule and not through the thalamus,¹⁷ lesion to direct corticonuclear connections cannot explain eyelid tremor in our patient. Indeed, both regions have additional reciprocal connections with the paramedian thalamus, in particular with the multiform and parvocellular divisions of the MD that show a high density of inhibitory GABAergic neurons.^{18–21} The MDpc is also connected to the rostral cingulate motor cortex—that is, the region that provides cortical input to the contralateral and ipsilateral intermediate subnucleus of the facial nucleus, which contains motoneurons for the OO.^{18,22} Here, the MDpc was clearly lesioned and is thus probably responsible for our patient's deficit, as none of the other affected nuclei has comparable connections to premotor structures involved in eyelid movements. We

hypothesise that lesion to the MDpc may have induced an excitatory-inhibitory disbalance between direct corticonuclear and indirect thalamus mediated signals for voluntary eye closure. Although very speculative, this hypothesis may also explain why comparable disorders are not seen with larger hemispheric lesions, as in such cases these direct and indirect pathways are damaged simultaneously.

In summary, this case shows that eyelid tremor may be a clinical sign of focal lesions affecting the paramedian thalamus, most probably the MDpc. It is noteworthy that inappropriate contractions of LP and OO with disturbed reciprocal inhibition similar to those observed in our patient have been recorded in a subgroup of patients with blepharospasm.¹ Our case thus lends further support to a possible role of the paramedian thalamus in the pathogenesis of this disorder.¹² However, it remains open whether the assumed inhibitory role of this region targets cortical regions involved in eyelid movements, other thalamic nuclei, or brain stem nuclei controlling LP and OO.

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Authors' affiliations

G J Jungehülsing, C J Ploner, Klinik für Neurologie, Charité, Humboldt-Universität, Berlin, Germany

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Correspondence to: Dr G J Jungehülsing, Klinik für Neurologie, Charité, Schumannstr 20/21, D-10117 Berlin, Germany; jan.junge-huelsing@charite.de

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